Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

# Regulatory Note REG2001-11

## Imidacloprid

The active ingredient imidacloprid and the formulated product, Admire 240 Flowable were first granted temporary registration in 1995 under Section 17 of the Pest Control Product Regulations. Admire 240 Flowable was used for the control of insecticide-resistant Colorado potato beetle in potatoes in eastern Canada. In the ensuing five years, several end-use products and a number of additional uses have been registered.

As proposed in Regulatory Note REG97-01, *Admire*, this regulatory note provides a summary of regulatory decisions taken regarding these products and of the rationales for these regulatory decisions.

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# Foreword

Health Canada's Pest Management Regulatory Agency (PMRA) first granted temporary registration for Admire 240 Flowable, containing imidacloprid, an insecticide developed by Bayer, which is effective against a broad spectrum of insects. The product was sold and used for the first time in Canada during the 1995 growing season for control of insecticide-resistant Colorado potato beetle in eastern Canada. In the ensuing five years, several end-use products, i.e., Admire, Gaucho, Merit and Advantage and a number of additional use sites, i.e., potato, apple, lettuce, tomato, mustard, canola, greenhouse cucumber, ornamental plants, turf and cats/dogs have been registered. As projected in REG97-01, *Admire*, this regulatory note provides a summary of regulatory decisions taken regarding these products and of the rationales for these regulatory decisions

Bayer was required to carry out additional chemistry, toxicological, residue and efficacy studies as a condition of these temporary registrations. Studies regarding environmental fate (groundwater monitoring in the U.S.) must still be completed. In addition, because of concerns regarding potential impacts on commercial pollinators, additional research is being conducted this growing season in Prince Edward Island and New Brunswick on the levels of imidacloprid residues in pollen and nectar from red clover, asters and goldenrod and whether imidacloprid residues are being carried back to the hive.

Regulatory limitations have been imposed with respect to imidacloprid primarily because of its potential to leach into surface and groundwater and to persist in soil. Review of additional data and information indicates that regulatory limitations continue to be necessary. A prudent approach is also necessary until the Agency has examined reports in the published literature and the results from studies being conducted this summer in Prince Edward Island concerning impacts on commercial pollinators. Imidacloprid use expansions will continue to be considered only for uses in low environmental risk situations or critical uses in the context of sustainable pest management programs where mitigative measures can be incorporated into product labelling to minimize known risks.

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## Introduction

In January, 1995, the Pest Management Regulatory Agency (PMRA) received several submissions requesting the registration of a new insecticidal active ingredient, imidacloprid, and the end use product, Admire 240 F, for use on potatoes, tomatoes and apples.

Through consultation with provincial extension personnel, user groups, and the registrant, Bayer Inc., the PMRA made a decision to initially focus a priority review on the use of imidacloprid for control of Colorado potato beetle (CPB) in potatoes. This approach was taken because of concerns over the critical pest management problems associated with CPB resistance to most insecticides that were then registered for its control.

In April, 1995, the PMRA granted temporary registration under section 17 of the Pest Control Products Regulations of Admire 240 F, for the control CPB in potatoes. Registration was conditional on the provision of further data to address concerns regarding persistence and mobility of the active ingredient in soil.

REG97-01, *Admire* discussed the initial registration decision, the limitations established related to expansion of the imidacloprid use pattern, and the data requirements needed to support continued registration and additional proposed uses. Since 1997, expansions of the imidacloprid use pattern have been considered where the criteria outlined in the regulatory note were met. Several end-use products formulated with imidacloprid and a number of uses are now registered. The registered imidacloprid use pattern is summarised in the attached Appendix I.

REG97-01, *Admire* indicated that use expansions to the imidacloprid use pattern could be considered where the following criteria are met: uses in low environmental risk situations (e.g., greenhouses, Saskatoon berries, seed dressings) and critical need uses which are linked to sustainable pest management programs and supported by provincial extension agencies. These criteria combined with temporary or time-limited registrations provide an opportunity for reconsideration and adjustment that may be necessary as more data become available.

This regulatory note provides a summary of decisions taken and of the rationales for the regulatory decisions regarding these products. The ongoing assessment of data, including studies generated in Canada, has confirmed the inherent properties of imidacloprid as identified in the original assessment and supports the continued judicious approach taken by the PMRA to use expansions to the imidacloprid use pattern.

Methods for analysing imidacloprid residues in environmental media are available to research and monitoring agencies upon request to the PMRA.

## Summary of Health Effects

In acute toxicity studies, technical imidacloprid was moderately toxic via the oral route and of low toxicity via the inhalation and dermal routes of exposure. It was non-irritating to the skin and eyes and it was not a skin sensitizer.

Short-term toxicity studies via the oral, dermal and inhalation routes did not reveal any adverse toxicological effects. Increased levels of mixed function oxidase were observed at high doses but in the absence of any other treatment-related findings, this was not considered to be an adverse effect. Summary evaluation of acute and subchronic neurotoxicity studies conducted with imidacloprid revealed no evidence of neuropathology.

Chronic toxicity studies did not result in any specific overt signs of intoxication, and there was no evidence of oncogenicity. In a battery of genotoxicity studies, the weight of the evidence suggests that imidacloprid is not genotoxic.

In reproductive and developmental toxicity studies, there was no evidence of adverse reproductive or teratogenic effects. Fetotoxicity was observed in rats and rabbits. In rabbits, the observed changes occurred at maternally toxic doses, and hence were considered to be secondary to maternal systemic toxicity. In rats, a slight increase in the incidence of a common observation (wavy ribs) was not deemed toxicologically significant.

In toxicokinetic studies, imidacloprid was rapidly excreted, with approximately 90% of the administered dose excreted within 24 hours. Urinary excretion accounted for 70-80% of the dose while faecal excretion accounted for 17-25% of the dose. There was no significant accumulation in the tissues at 48 hours and only trace amounts were detected in expired air.

Occupational and bystander exposure assessments have been conducted to estimate potential exposure to imidacloprid. For the turf use, for example, passive dosimetry monitoring of adults during a choreographed routine on treated turf, as well as determination of residues available for transfer, were reviewed. The results of these studies provided estimates of dermal, inhalation and non-dietary ingestion exposure for children contacting treated turf during play.

The PMRA has conducted dietary and occupational/bystander risk assessments for registered uses of imidacloprid and risk levels are acceptable.

In October, 1999, the U.S. EPA published a Data Call-In for pesticides thought to have neurologic effects. Imidacloprid is among a class of insecticides, the neonicotinoids, whose mode of action is via a neurologic mechanism in insects. In their assessment, the U.S. EPA concluded that although there was no evidence of sensitivity in fetuses as compared to maternal animals following *in utero* exposure in rats and rabbits, the additional *Food Quality Protect Act* safety factor would be retained but reduced to 3× with a requirement for the registrant to conduct a developmental neurotoxicity study. The PMRA will harmonize with this requirement by requesting the data at the same time.

## Summary of Environmental Effects

As indicated in REG97-01, *Admire*, the Agency requested more data regarding the environmental impact of imidacloprid including studies on its toxicity to birds and aquatic organisms, terrestrial field dissipation, runoff modelling and groundwater monitoring studies. Additional data have been received and reviewed. These data confirm initial findings regarding the persistence, potential mobility and toxicity to non-target organisms of imidacloprid. With respect to the groundwater monitoring studies, interim reports have been provided and final reports are anticipated. PMRA will continue to review this additional information as well as any other studies that are submitted and will report any new findings.

Imidacloprid is classified as persistent under agricultural field crop conditions according to the classification scheme of Goring *et al.* (1975), with a $DT_{50}$ in soil in the order of 1-2 years. The term $DT_{50}$ refers to the time it takes for 50% of the applied pesticide to dissipate in the soil.

By way of comparison, atrazine, with a $DT_{50}$ of 120 days, is classified as moderately persistent; diazinon, with a $DT_{50}$ of 40 days, is classified as slightly persistent; and acephate, with a $DT_{50}$ of 3 days, is classified as non-persistent using the same classification scheme (see Table 1).

With a $DT_{50}$ of 21-33 days in turf-covered soils such as golf course/orchard settings, persistence of imidacloprid in soil is reduced in comparison to agricultural field crop conditions. The time for 90% of the applied imidacloprid to dissipate in turf-covered soil (i.e., $DT_{90}$), however, was in the order of 1.2-2 years. This result indicated that, while imidacloprid may be classified as slightly persistent in turf based on the $DT_{50}$ values, the $DT_{90}$ values indicate higher persistence and a potential for carryover in turf-covered soil.

Imidacloprid is strongly bound to soils in which it has been allowed to age for 4-8 weeks after application. The persistence of imidacloprid may lead to accumulation of residues from repeat applications. It is assumed that soils do not have an infinite capacity to bind imidacloprid. Therefore if the binding capacity of the soil is reached, aged imidacloprid may leach into groundwater. Bayer recognizes the complexity of the soil sorption issues surrounding imidacloprid and is currently evaluating its own experimental database and

published literature related to binding of imidacloprid by soil. Bayer will provide the results of this analysis to the PMRA.

The compound is highly soluble in water. Thus, freshly applied or unbound imidacloprid is subject to initial runoff. The physical/chemical properties of imidacloprid suggest a high leaching potential. Modelling systems, such as the Expert System for Pesticide Regulatory Evaluations and Simulations (EXPRES), that incorporate product characteristics including solubility, persistence, and binding to soil can be used to compare the leaching attributes of imidacloprid with registered pesticides whose characteristics have become recognized through long years of use.

Although the U.S. EPA reached similar conclusions, they have taken a different approach in terms of acceptable use expansions requiring that groundwater monitoring studies be conducted to measure leaching under actual use conditions. Bayer is nearing completion of prospective groundwater studies over 4.5 years in California and Michigan with involvement of the U.S. EPA. The studies were performed in sandy agricultural fields in Salinas Valley, California, and Vestaberg, Michigan, overlying shallow groundwater, and therefore reflect mobility and potential for groundwater contamination in highly vulnerable settings. Bayer is also working with officials in Suffolk County, Long Island to conduct a general groundwater monitoring program in areas of agricultural and horticultural use.

Interim results submitted in 1998 by the registrant indicate that, after three years of use, low concentrations of imidacloprid and its metabolites were detected at sites in New York and Michigan. Bayer will provide final study reports to the PMRA when available. There is no practical remedial action that can be taken once groundwater is contaminated with a pesticide. This is of concern because groundwater can recharge wetlands and surface waters, especially in areas with a shallow groundwater table.

Groundwater monitoring studies conducted in Ontario and Quebec in 1996 and 1997 by the provincial authorities did not indicate leaching of imidacloprid or its metabolites through the soil. Trace concentrations of imidacloprid, however, were detected in groundwater from a single well adjacent to a potato field in Prince Edward Island. However, more recent sampling has not shown any additional detections of the chemical in that well.

Studies on experimental test plots and spot sampling of commercial agricultural treatments in the Atlantic provinces show concentrations of imidacloprid in runoff water. *Ad hoc* monitoring of tile drains in Ontario also have shown low concentrations of imidacloprid in surface runoff water. Surface runoff potential is relevant to aquatic non-target organisms. The concentrations of imidacloprid detected in surface runoff water in the Atlantic provinces in studies mentioned above have the potential to impact aquatic invertebrate indicator species in streams and ponds.

Imidacloprid has a broad spectrum of activity against a wide range of arthropods including pests, parasites, predators of pests, and aquatic invertebrates.

Although recognized as a highly persistent material in field crop settings, imidacloprid does not bioaccumulate as do chlorinated hydrocarbons. Imidacloprid is toxic to birds on an acute and reproductive effects basis. Precautionary statements regarding toxicity to birds are required on product labels.

PMRA's initial review concluded that, although pollinators could be at risk because of high toxicity of imidacloprid to bees exposed to direct treatment, or residues on blooming crops or weeds, this risk could be mitigated by a label statement contraindicating application of the product to blooming crops when bees are visiting the treatment area.

Since that time, the question of whether systemic residues of imidacloprid may occur in nectar and pollen of flowering crops at concentrations harmful to bees has been the focus of an extensive research program. PMRA will be reviewing as a priority relevant studies from the published literature and elsewhere to determine whether imidacloprid is the cause of adverse effects and mortalities of commercial pollinators.

**Table 1 A comparison of persistence, solubility and mobility characteristics of imidacloprid with selected pesticides, using the EXPRES model.**

| Ranked in order of | | | |
|---|---|---|---|
| $DT_{50}$ (days) | Solubility (g/L) | Leaching Potential[¶] (score) | Leaching Index[§] (score) |
| **Imidacloprid** (426) | Acephate (650) | Acephate ($1.42 \times 10^{6}$) | Acephate ($4.25 \times 10^{6}$) |
| Dimethoate (122) | Dimethoate (25) | **Imidacloprid** ($9.96 \times 10^{3}$) | **Imidacloprid** ($4.24 \times 10^{6}$) |
| Atrazine (120) | **Imidacloprid** (0.51) | Dimethoate ($1.14 \times 10^{3}$) | Dimethoate ($1.39 \times 10^{5}$) |
| Diazinon (40) | Malathion (0.15) | Atrazine ($5.45 \times 10^{0}$) | Atrazine ($6.54 \times 10^{2}$) |
| Acephate (3) | Diazinon (0.040) | Malathion ($1.59 \times 10^{-2}$) | Diazinon ($8.42 \times 10^{-2}$) |
| Malathion (1) | Atrazine (0.033) | Diazinon ($2.11 \times 10^{-3}$) | Malathion ($1.59 \times 10^{-2}$) |

Notes:

¶ Potential to migrate through unsaturated zone to the water table.

§ Based on extent of the potential migration distance of the pesticide, i.e. how far it will migrate before degrading.

## Summary of Regulatory Rationales for Approved Uses of Imidacloprid

A number of additional uses for imidacloprid have been approved since the initial registration of this insecticide in 1995. These uses and the rationales for their approval are discussed here and summarised in the attached Appendix I. Other uses also have been proposed but were found not to meet the criteria outlined in REG97-01, *Admire*.

**Colorado Potato Beetle in Potato, Tomato; Spotted Tentiform Leafminer in Apple:** The initial imidacloprid registration was granted for control of the CPB in potato in eastern Canada and secondly for control of spotted tentiform leafminer (STLM) in apple in response to severe widespread insecticide resistance to registered products in these pests. Registration was subsequently extended to include tomato, another host of CPB and to allow these uses across Canada. A maximum of a single in-furrow application (in potatoes) or two foliar applications per season and other precautionary measures were incorporated into use directions of the product label to preclude or delay the development of CPB and STLM resistance to imidacloprid.

**Aphid in Field Lettuce:** Use to control aphid pests, particularly lettuce aphid, was first approved in British Columbia as no effective alternative product was available. Without effective treatment, losses of up to 25% of the crop can be expected. This use was also extended across Canada as other lettuce-growing areas in Canada experienced similar needs.

**Aphid and Whitefly in Greenhouse-Grown Plants (vegetable and ornamental); Flea Adulticide (cats and dogs):** Limited risk of environmental exposure was anticipated with these uses allowing consideration of Merit and Impower for greenhouse use and Advantage for use on domestic pets.

**Seed Treatment in Canola, Corn:** The insecticide lindane which was widely used as a prophylactic flea beetle seed treatment has come under international regulatory scrutiny and is under special review in Canada. Initially, the PMRA granted registration of imidacloprid as a lindane replacement for treatment of canola seed for export only. Registration was then extended for use on canola seed planted in Canada on the condition that additional supervised residue trials be conducted. This condition has now been met. An assessment of the potential risk to birds from seed treatment use of imidacloprid indicated lower risk to birds compared to granular insecticides. The relatively low application rates (grams active ingredient per hectare) associated with seed treatments were also taken into consideration in permitting this use. Registration for control of corn flea beetle on field corn was granted in May 2001.

**European Chafer, Japanese Beetle in Turf in Ontario and Quebec:** The currently registered alternative products for this use are the organophosphate insecticides, chlorpyrifos and diazinon and the carbamate, carbaryl. These insecticides are not as effective as imidacloprid for a number of reasons including their shorter persistence and the probable resistance in the target pests to these insecticides. Additional concerns such as the relative potential for bystander and applicator exposure and the redundant application of diazinon and chlorpyrifos by users trying to overcome the performance limitations of these products were also considered.

## Conclusion

Imidacloprid has value in controlling pests which have become resistant to other insecticides and as a potential replacement to insecticides that are under reevaluation. Nevertheless its potential to disrupt established integrated pest management (IPM) programs, to engender resistance in some species if used to excess, its broad spectrum of activity and its potential for mobility and persistence in the environment have led the PMRA to adopt the current regulatory approach to this insecticide. Imidacloprid use expansions are considered only in the context of sustainable pest management programs and where mitigative measures can be incorporated into product labelling. The PMRA recognizes the contribution that provincial regulatory and extension personnel and other expert advisors can make to user compliance with these measures.

The PMRA acknowledges the importance of working in partnership with grower organizations and experienced extension specialists as well as pesticide manufacturers, to strengthen IPM programs and manage the use of this insecticide.

Regulatory limitations have been imposed with respect to imidacloprid because of its potential to leach into surface and groundwater and to persist in soil. Review of additional data and information indicates that these regulatory limitations continue to be necessary. The PMRA will continue its judicious regulatory approach to imidacloprid. PMRA will continue to review additional information as well as any other studies that are submitted and will report any new findings.

In conclusion, imidacloprid use expansions will continue to be considered only for uses in low environmental risk situations or critical need uses in the context of sustainable pest management programs and where mitigative measures can be incorporated into product labelling.

## References

Goring, C. A. I., D. A. Laskowski, J. H. Hamaker, and R. W. Meikle. 1975. Principles of pesticide degradation in soil. pp. 135-172 in R. Haque and V. H. Freed, eds. Environmental Dynamics of Pesticides. Plenum Press, New York.

# Appendix I Summary of approved uses of imidacloprid

| Crop | Pest | Rate | Date First Registered / Renewal Date | Comments |
|---|---|---|---|---|
| **Admire 240 F, Reg. No. 24094** | | | | |
| potato | Colorado potato beetle | 48 (foliar)-312 (in-furrow) g a.i./ha Maximum 312 g a.i. in-furrow **or** 2 foliar (2 X 48 g a.i.) applications per season. | April 28, 1995 - Dec 31, 2001 | First registered for use to control CPB in potatoes in eastern Canada in 1995.<br><br>Approved for use in potatoes across Canada, April 21, 1999. |
| apple | apple; rosy apple aphids<br>white apple leafhopper<br>mullein bug<br>tentiform leafminer | 55 g a.i./ha<br>48 g a.i./ha<br>91 g a.i./ha<br>91 g a.i./ha<br>Maximum 2 foliar applications per season. | July 27, 1997 - Dec 31, 2001 | First registered for use Quebec and Ontario, addition of BC in 1998. |
| lettuce | aphid | 48 g a.i./ha (foliar); 156 - 312 (soil drench) g a.i./ha **or** 2.5 g a.i./1000 seedlings as transplant plug drench. Maximum 312 g in furrow **or** 2 foliar applications per season | August 20, 1999 - Dec 31, 2001 | First approved for use on field lettuce in British Columbia August 20, 1999 and extended for use in other lettuce-growing areas in Canada Dec. 17, 1999. |
| tomato | Colorado potato beetle | 48 (foliar)-312 (in-furrow) g a.i./ha Maximum 312 g in furrow **or** 2 foliar applications per season | April 15, 1996 - Dec 31, 2001 | Approved for use on field tomato in eastern Canada only. |
| **Gaucho 75 ST, Reg. No. 25556**<br>**Gaucho 480 F, Reg. No. 26124** | | | | |
| mustard, canola | flea beetle | 394-787 g a.i./100 kg seed | Oct 26, 1999 - Dec 31, 2001 | Treatment of seed for export to the US with Gaucho 75 ST was first registered 1998.<br><br>Treatment of seed for use in Canada, 1999. |

| Crop | Pest | Rate | Date First Registered / Renewal Date | Comments |
|---|---|---|---|---|
| field corn | corn flea beetle | 254 g a.i./100 kg seed | May 10, 2001 | Gaucho 480 F approved for temporary use on corn seed until July 2001. |
| **Merit 60 WP Greenhouse Insecticide, Reg. No. 25636<br>Impower 60 WP Greenhouse Insecticide, Reg. No. 25658** | | | | |
| cucumber, tomato, vegetable (greenhouse) | aphid<br>whitefly | 9.6 g a.i./1000 plants in 1000 L water | July 21, 1998 - Dec 31, 2003 | Limited environmental risk. |
| ornamental plants (container grown) | aphid<br>whitefly | 8.0 g a.i./1000 L<br>0.002-0.003 g a.i./pot | July 21, 1998 - Dec 31, 2003 | Limited environmental risk. |
| **Merit Solupak Insecticide 75 % WP, Reg. No. 25932<br>Merit 0.5 G Insecticide, Reg. No. 25933** | | | | |
| airport, recreational area, lawn, turf | European chafer<br>Japanese beetle | 330 g a.i./ha | June 30, 1999 - Dec 31, 2001 | Approved for use in Ontario and Quebec only. Registration granted conditional on providing environment fate data in urban settings. |
| **Advantage Flea Adulticides, Reg. Nos. 25127, 25128, 24129, 25130, 25131, 25132** | | | | |
| cats, dogs | adult fleas | | June 23, 1997 - Dec 31, 2002 | Limited environmental risk; full registration |